REMARKS

Claims 1-78 were pending in the application. Claims 1-33 and 44-77 have been cancelled. Accordingly, upon entry of the present amendment, claims 34-43, and 78 will be pending in the instant application.

Any cancellation of the claims should not be construed as an acquiescence to any of the rejections set forth in the instant Office Action, and were done solely to expedite prosecution of the application. Applicants hereby reserve the right to pursue the subject matter of the claims as originally filed in this or a separate application(s).

Rejection of Claims 34-36, 38-43, and 78 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 34-36 and 38-43, and 78 under 35 U.S.C. §112, first paragraph, "because the specification, while being enabling for the direct measurement of PGC-1 expression as in claim 37, does not reasonably provide enablement for the use of surrogates such as glucose output or expression of one of phosphoenolpyruvate carboxykinase, glucose-6-phosphate or fructose-1,6- bisphosphatase as in claims 38-41." Furthermore, the Examiner points to the Wands Factors, and is of the opinion that, with respect to the breadth of the claims, "[t]he claims encompass the use of any surrogate for analysis of PGC-1 including those specifically identified in claims 40 and 41."

Applicants respectfully traverse the foregoing rejection. Applicants maintain that one of ordinary skill in the art would be able to make and use the claimed invention using only routine experimentation. Applicants submit that the specification is enabling for methods to identify a compound that modulates gluconeogenesis by assaying the ability of the compound to modulate the expression of a PGC-1 nucleic acid molecule or the activity of a PGC-1 polypeptide (claim

34), as well as assaying the ability of a compound to modulate interaction between the PGC-1 protein and the target molecule to thereby identify a compound which modulates gluconeogenesis (claim 78).

More specifically, claim 34, is directed to a method for identifying a compound capable of modulating gluconeogenesis comprising contacting a cell with a compound, and ***assaying the ability of the compound to modulate the expression of a PGC-1 nucleic acid molecule or the activity of a PGC-1 polypeptide***, to thereby identify a compound that modulates gluconeogenesis. In other words, claim 34 requires a direct measurement of the expression of a PGC-1 nucleic acid molecule or the activity of a PGC-1 polypeptide.

The Examiner's comments appear to be directed to the Examiner's position that the use of surrogates to identify a modulator of gluconeogenesis is not enabled. Claim 34 is not directed to the use of surrogates. Rather, claim 34 requires the measurement of ***PGC-1 expression*** or ***PGC-1 activity***. Applicants further submit that based on the teachings and guidelines of the present invention as disclosed in the application, in combination with the knowledge of one of skill in the art at the time the application was filed, the procedures for assaying the ability of the compound to modulate the ***expression of a PGC-1 nucleic acid molecule*** or the ***activity of a PGC-1 polypeptide*** are routine to one skilled in the art and are not limited to Northern blotting as asserted by the Examiner. For example, at page 69, lines 20-24 of the instant specification, methods to detect PGC-1 mRNA or protein are described:

> the detection method of the invention can be used to detect PGC-1 mRNA or protein in a biological sample in vitro as well as in vivo. For example, in vitro techniques for detection of PGC-1 mRNA include Northern hybridizations and in situ hybridizations. In vitro techniques for detection of PGC-1 protein include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence.

Moreover, numerous additional methods for measuring the expression of PGC-1 or the activity of PGC-1 would have been known to one of ordinary skill in the art at the time the application was filed.

Claim 78 is directed to a method for identifying a compound which modulates gluconeogenesis, comprising: a) providing a PGC-1 protein or biologically active fragment thereof and a target molecule, wherein the target molecule is HNF-4α or the phosphoenolpyruvate carboxykinase promoter; b) incubating the PGC-1 protein or biologically active fragment thereof and the target molecule in the presence of a compound under conditions which allow binding of the target molecule to the PGC-1 protein to form a complex; and c) detecting the formation of a complex of the PGC-1 protein and the target molecule in which the ability of the compound to modulate interaction between the PGC-1 protein and the target molecule is indicated by a modulation in complex formation in the presence of the test compound as compared to the modulation of the complex formed in the absence of the compound, to thereby identify a compound which modulates gluconeogenesis. Applicants respectfully submit that the specification provides ample basis to verify that the measurement of binding of PGC-1 to HNF-4 or the PEPCK promoter is sufficient to identify a compound which modulates gluconeogenesis (see, for example, the section entitled Screening Assays, at page 60 through page 68 of the specification). In addition, Applicants provide a working example to demonstrate that PGC-1 interacts with AF1 sites on HNF-4α and the PEPCK promoter, both of which are intimately involved with gluconeogenesis (see, Example 4, page 79 to page 85 of the specification).

With respect to dependent claims 38-41, the Examiner states that "[t]he specification, while suggesting the use of surrogate reporter systems, does not provide sufficient basis to verify whether these surrogates will function to show a change in the expression or activity of PGC-1". Applicants

respectfully traverse this rejection and remind the Examiner that these claims are ***dependent*** and thus must be read in light of the independent claim they depend upon, *i.e.*, claim 34, a claim directed to a screening assay. The fact that some false positives ***may be*** produced by the claimed methods as defined in claims 38-41, does not render the claims unpatentable, *per se*. Again, the Examiner is reminded that the claims are directed to screening assays. Applicants further submit that one of skill in the art would know how to confirm whether a compound that is identified using the surrogates of claim 38 actually modulates the expression or activity of PGC-1, *e.g.*, with Northern hybridizations, *in situ* hybridizations, enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. Applicants therefore submit that the specification is enabling for the claimed methods, *i.e.*, assaying the ability of the compound to modulate the expression of a PGC-1 nucleic acid molecule or the activity of a PGC-1 polypeptide, to thereby identify a compound which modulates gluconeogenesis, whether or not a surrogate is employed in these methods. Reconsideration and withdrawal of the §112, first paragraph rejection is thus requested.

Rejection of Claims 34-37 and 41-43 Under 35 U.S.C. §102

Applicants note the withdrawal of the rejection of claims 34-37 and 41-43 under 35 U.S.C. §102.

Rejection of Claims 34-37 and 41-43 Under 35 U.S.C. §103(a)

Applicants note the withdrawal of the rejection of claims 34-37 and 42-43 under 35 U.S.C. §103(a).

CONCLUSION

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the examiner is urged to call the undersigned at (617) 227-7400.

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Respectfully submitted,

By _____

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